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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/050,088	01/14/2002	Robert C. Getts	4081.010	6251

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EXAMINER
CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/050,088	Getts
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 14, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-24* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

2. Claims 1-3, 6-8, 12, and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Hellyer et al. (U.S. Patent 6,207,818 B1) (March 27, 2001).

Hellyer et al teach a method for determining the presence of at least one specific nucleotide sequence in a target nucleic acid reagent extracted from a biological sample (abstract), the method comprising the steps of:

a) concurrently contacting a microarray with:

(I) a target nucleic acid reagent, the target nucleic acid reagent having a nucleotide sequence, the nucleotide sequence further including a capture sequence (Column 16, lines 1-40, and Example 5);

(ii) a capture reagent, the capture reagent having at least one first arm having a label capable of emitting a detectable signal and at least one second arm having a nucleotide sequence complementary to the capture sequence of the target nucleic acid reagent (Example 5);
the microarray having thereon a plurality of features, each of the plurality of features including a probe nucleotide sequence; and

b) treating the microarray from step a) at a temperature and for a time sufficient to induce the nucleotide sequence of the target nucleic acid to hybridize to the probe nucleotide sequence complementary thereto on the microarray, and to induce the capture reagent to hybridize to the capture sequence of the nucleotide sequence of the target nucleic acid hybridized to the microarray (Example 5, and Column 13, line 63 to column 14, line 9).

Hellyer et al teach a method, wherein the presence of the latter hybridization results in the emission of the detectable signal from the corresponding feature, and in the absence thereof results in no emission of the detectable signal from the corresponding feature, thus generating a detectable hybridization pattern for subsequent analysis (Column 16, lines 24-40, and Example 5).

Hellyer et al teach a method, wherein the microarray is incubated at a first temperature for a first period of time and thereafter at a lower second temperature for a second period of time which may be different than the first period of time that are suitable for hybridization of the target nucleic acid reagent to the capture reagent (Example 5).

Hellyer et al teach a method, further comprising the step of utilizing a spin column to prepare the target nucleic acid reagent prior to step (a) ((Example 5, column 20, lines 28-30).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 9-11, 16, 18, 19, and 23 are rejected under 35 U.S.C. 103(a) over Hellyer et al. (U.S. Patent 6,207,818 B1) (March 27, 2001).

Hellyer et al teach the method of claims 1-3, 6-8, 12, and 24 as described above in detail.

Hellyer et al do not teach the method, wherein the first temperature ranges from 65 degree centigrade to 75 degree centigrade or about 32 degree centigrade and the second temperature ranges from 50 degree centigrade to 55 degree centigrade and the first period of time is overnight and the second period of time is 4 to 6 hours.

However, it is *prima facie* obvious that selection of the specific temperature and time period of a nucleic acid hybridization reaction represent routine optimization with regard to sequence, length and compositions of the DNA sequences being screened as well as the size and sequence of the capture molecule and the requirement of screening speed which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of the specific temperature and time period of a nucleic acid hybridization reaction performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

7. Claim 5 is rejected under 35 U.S.C. 103(a) over Hellyer et al. (U.S. Patent 6,207,818 B1) (March 27, 2001) in view of Kayyem et al. (U.S. Patent 6,290,839 B1)(September 18, 2001).

Hellyer et al teach the method of claims 1-3, 6-12, and 16, 18, 19, and 23-24 as described above.

Hellyer et al do not teach the method wherein the capture reagent is a dendrimer.

Kayyem et al teach the method wherein the capture reagent is a dendrimer (Column 52, lines 27-43, and column 59, lines 18-42).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the capture reagent is a dendrimer of Kayyem et al in the method of Hellyer et al , since Kayyem et al. state, "Adding extra linking sequences between the probe nucleic acid and the ETMs can result in the ETMs being spatially closer to the surface, giving better results (Column 59, lines 31-34)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein the capture reagent is a dendrimer of Kayyem et al in the method of Hellyer et al in order to improve the process for determining the presence of at least one specific nucleotide sequence in a target nucleic acid and also in order to achieve the express advantages, as noted by Kayyem et al., of an invention which provides addition of extra linking sequences between the probe nucleic acid and the ETMs that can result in the ETMs being spatially closer to the surface, giving better results.

8. Claims 4, 13-15, 17, and 20-22 are rejected under 35 U.S.C. 103(a) over Hellyer et al. (U.S. Patent 6,207,818 B1) (March 27, 2001) in view of Lipshutz et al. (U.S. Patent 6,280,950 B1) (August 28, 2001).

Hellyer et al teach the method of claims 1-3, 6-12, and 16, 18, 19, and 23-24 as described above.

Hellyer et al do not teach the method wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence.

Lipshutz et al teach the method wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence (Column 8, lines 13-36).

Hellyer et al do not teach the method wherein the first temperature of hybridization is below the melt temperature of the blocking oligonucleotide and the second temperature of hybridization is above the melt temperature of the blocking oligonucleotide.

Lipshutz et al teach the method wherein the temperature of hybridization can be optimized depending on the length and sequence of the target nucleic acid (Column 7, lines 9-33).

Hellyer et al do not teach the method wherein the target nucleic acid is cDNA.

Lipshutz et al teach the method wherein the target nucleic acid is cDNA (Column 9, line 62 to column 10, line 13).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence and the optimization of hybridization temperature depending on the length and sequence of the target nucleic acid of Lipshutz et al. in the method of Hellyer et al., since Lipshutz et al. state, "For example, when it is desired to detect a particular (target) nucleic acid that is expressed at low levels in a nucleic acid sample, selective elimination of other nucleic acids that are present in high level in the sample can improve detection and isolation of the target sequence. In this case, a

nucleic acid pool containing nucleic acids complementary to the nucleic acids it is desired to block in the sample can be hybridized to the sample. The nucleic acid pool (blocking reagent) will hybridize to complementary sequences in the sample, form stable hybrid duplexes, and thereby prevent interaction (e.g., nonspecific binding) of the blocked nucleic acids with the capture sequence (Column 8, lines 17-29)." By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein a blocking oligonucleotide is utilized prior to the hybridization of the capture reagent with the target nucleic acid sequence and the optimization of hybridization temperature depending on the length and sequence of the target nucleic acid of Lipshutz et al. in the method of Hellyer et al., in order to improve the process for detection of a target nucleic acid and also in order to achieve the express advantages, as noted by Lipshutz et al., of an invention which provides prevention of interaction (e.g., nonspecific binding) of the blocked nucleic acids with the capture sequence and selective elimination of other nucleic acids that are present in high level in the sample thereby improving detection and isolation of the target sequence.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this

Group is (703) 305-7401. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

February 26, 2003

ARUN K. CHAKRABARTI
PATENT EXAMINER